



UNITED STATES DEPARTMENT OF COMMERCE
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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
|-----------------|-------------|----------------------|---------------------|

09/605, 577 06/28/00 WANG

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HM22/0313

EXAMINER

JAMES A GIBLIN
BAYER CORPORATION
800 DWIGHT WAY
BERKELEY CA 94701

SEHARASEYON, T

ART UNIT

PAPER NUMBER

1647

DATE MAILED:

03/13/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILE COPY

| | | |
|------------------------------|-------------------------|---------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/605,577 | WANG ET AL. |
| | Examiner | Art Unit |
| | Jegatheesan Seharaseyon | 1647 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 31 January 2001.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-6, 9 and 10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-6, 9 and 10 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) Notice of References Cited (PTO-892) 18) Interview Summary (PTO-413) Paper No(s). _____ .
- 16) Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) Notice of Informal Patent Application (PTO-152)
- 17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . 20) Other: _____ .

DETAILED ACTION

1. This office action is in response to your amendments filed 1/31/2001. Claims 1-6, 9 and 10 are pending and are rejected.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because all the inventors names have to be on the same sheet.

3. The claims rejection made under 35 USC § 112, first and second paragraph are withdrawn in light of applicants amendments.

4. The rejection of claims 1-6 under 35 USC § 103 as being obvious over Hora et al. (U.S. Patent No. 5,078,997), in view of Lee (U.S. Patent No. 5,65,730) is maintained. Applicants arguments have been fully considered but are not deemed to be persuasive. Applicant argues that although Hora et al. list amino acids as stabilizers it is known that not all amino acids stabilize proteins. They cite Taneja et al. (1994) and Rishi et al (1998) to support their argument. However, Taneja et al. (1994) and Rishi et al. (1998), evaluated the stability of cytochrome C and other proteins in the presence of histidine in a citrate buffer containing KCl. These references are not relevant as the solutions lacked any sugars. As set forth in the previous office action, the stabilizing effect of histidine is in the presence of sugars such as sucrose. Hora et al. teaches stabilization of IL-2 with sugars, amino acids etc., and Lee discloses the use of sucrose and histidine

to stabilize monomeric proteins. Therefore, the claims are obvious over Hora et al. (U.S. Patent No. 5,078,997), in view of Lee (U.S. Patent No. 5,65,730).

5. The rejection of claims 9 and 10 under 35 USC § 103 as being obvious over Hora et al. (U.S. Patent No. 5,078,997), in view of Nayar (U.S. Patent No. 5,874,408) is maintained. Applicants arguments have been fully considered but are not deemed to be persuasive. Applicant argues that although Nayar shows the use of histidine (with other substances) to stabilize factor VIII, there is no suggestion in that reference that histidine could be used as a stabilizer for interleukins. The teachings of Hora et al. and Nayar are set forth in Paper No: 3. Nayar teaches that the destabilizing effects of histidine can be effectively overcome by a novel formulation of salts, glycine and sucrose (column 2, lines 64-67). Although Nayar does not teach stabilization of interleukins, his teachings motivate one of ordinary skill in the art at the time the instant invention was made to modify the composition disclosed in Hora et al. by adding the additional elements disclosed in Nayar. Therefore, the claims are obvious over Hora et al. (U.S. Patent No. 5,078,997), in view of Nayar (U.S. Patent No. 5,874,408).

6. The following is a new ground of rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6a. Claims 1-6 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Shanafelt et al. (WO 996018 A1).

The instant invention is directed to stable lyophilized pharmaceutical compositions of Interleukin-2 or a variant (N88R) stabilized by histidine, salts and sugar having an aqueous pH ranging from about 5.0 to about 6.5.

Shanafelt et al. (WO 996018 A1) teach IL-2 muteins (including N88R) in pharmaceutical compositions formulated by well known methods (page 20, lines 25-30). The pharmaceutical compositions of the IL-2 mutein may be formulated in a variety of forms including lyophilization (page 20, lines 25-30). Thus, the instant invention is anticipated by Shanafelt et al. (WO 996018 A1).

7. No claims are allowed.

Contact Information.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



JEFFREY STUCKER
PRIMARY EXAMINER

JS

March 9, 2001